

Table of the oversight of biotechnology products and relevant coordination across EPA, FDA, and USDA:

This table summarizes current responsibilities and the relevant coordination across USDA, EPA, and FDA for the regulatory oversight of biotechnology products. The contents of the table are draft and still under review at the various agencies. When the contents are finalized, the table will be incorporated into the update to the Coordinated Framework, which will undergo a formal public comment period. While the information in this table is intended to be as comprehensive and accurate as possible, it should not be construed to impair or otherwise affect the agency mission as established by law for each agency or the authority granted by law to each agency or the head thereof. Also, the information in the table should not be interpreted as a guarantee that specific products in any of the areas specified have been in the past, or will be in the future, determined to be safe by the relative regulatory agencies. The table does not specify the applicable regulatory requirements or procedures, which may vary depending on the product. The table does not identify additional government agencies and associated requirements that may be relevant to products imported into the United States for marketing or investigation. Products imported into the United States must meet all applicable requirements, including any import certification or permit requirements. Also note that the inclusion of a product area in this table does not indicate the existence of commercially available products or endorsement of the development of such products by the Federal government.

Agency Acronyms

EPA		<u>Environmental Protection Agency</u>
	OPP	Office of Pesticide Programs (EPA)
	OPPT	Office of Pollution Prevention and Toxics (EPA)
	TSCA	Toxic Substance Control Act (EPA)
FDA		<u>Food and Drug Administration</u>
	CBER	Center for Biologics Evaluation and Research (FDA)
	CDER	Center for Drug Evaluation and Research (FDA)
	CDRH	Center for Devices and Radiological Health (FDA)
	CFSAN	Center for Food Safety and Applied Nutrition (FDA)
	CVM	Center for Veterinary Medicine (FDA)
USDA		<u>Department of Agriculture</u>
	APHIS	Animal and Plant Health Inspection Service (USDA)
	BRS	Biotechnology Regulatory Services (USDA/APHIS)
	PPQ	Plant Protection and Quarantine (USDA/APHIS)
	VS	Veterinary Services (USDA/APHIS)
	CVB	Center for Veterinary Biologics (USDA/APHIS/VS)

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Oversight of biotechnology products and relevant coordination across EPA, FDA, and USDA

Product Area	Source Organism or Culture		
	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Food for humans	<u>USDA/APHIS/BRS</u> ¹ If GE plant poses a plant pest risk <u>FDA/CFSAN</u> ² <u>EPA/OPP</u> If plant-incorporated protectant is produced by GE plant, EPA/OPP regulates the pesticide trait and related genetic material for human and environmental safety and for pesticide residue food/feed safety	<u>FDA/CVM</u> ³ <u>USDA/APHIS/BRS</u> If GE animal poses a plant pest risk <u>USDA/APHIS/VS</u> If GE animal poses health risk to livestock ⁴	<u>FDA/CFSAN</u>

¹ USDA/APHIS/BRS oversees the importation, interstate movement, and environmental release of the GE plants (that pose a plant pest risk) that are used for food purposes. USDA/APHIS does not regulate activities in confined facilities such as laboratories and greenhouses.

² FDA has a voluntary food safety and regulatory consultation process for human and/or animal foods derived from GE plant varieties to be used in the general food supply, and strongly recommends that all developers of such products partake in the consultation process early in the development process. Particular uses of foods (including food substances) may be subject to certain premarket requirements. The fact that a food or food substance does or does not come from a GE plant has no bearing on those requirements.

³ FDA/CVM is responsible for reviewing and approving the safety and effectiveness of the introduced genomic alteration in the animal, including animal health, human and animal food safety, and whether the desired trait is expressed. Please see *FDA Guidance for Industry 187*, available at <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf>.

⁴ Livestock includes horses, cattle, bison, sheep, goats, swine, cervids, poultry, and other farm-raised animals, including farm-raised fish.

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Product Area	Source Organism or Culture		
	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Food for animals	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>FDA/CVM</u> <u>EPA/OPP</u> If plant-incorporated protectant is produced by GE plant, EPA/OPP regulates the pesticide trait and related genetic material for human and environmental safety and for pesticide residue food/feed safety	<u>FDA/CVM</u> <u>USDA/APHIS/BRS</u> If GE animal poses a plant pest risk <u>USDA/APHIS/VS</u> If GE animal poses health risk to livestock ⁴	<u>FDA/CVM</u>
Drug for humans	<u>FDA/CDER</u> <u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk	<u>FDA/CVM</u> <u>FDA/CDER</u>	<u>FDA/CDER</u>
Biological product for humans	<u>FDA/CBER</u> or <u>FDA/CDER</u> ⁵ <u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk	<u>FDA/CVM</u> <u>FDA/CBER</u> or <u>FDA/CDER</u>	<u>FDA/CBER</u> or <u>FDA/CDER</u>
Medical device or medical diagnostic for humans	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>FDA/CDRH</u>	<u>FDA/CVM</u> <u>FDA/CDRH</u>	<u>FDA/CBER</u> or <u>FDA/CDRH</u> ⁶

⁵ FDA/CBER and FDA/CDER each have regulatory responsibility, including pre-market review and oversight, for human biological products. For information regarding the division of regulatory responsibility for human biological products between FDA/CBER and FDA/CDER, please see *Transfer of Therapeutic Products to the Center for Drug Evaluation and Research (CDER)*, available at <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133463.htm>.

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	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Drug for animals	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>FDA/CVM</u>	<u>FDA/CVM</u>	<u>FDA/CVM</u>
Biological product for animals (veterinary biological product)	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>USDA/APHIS/VS/CVB</u>	<u>FDA/CVM</u> If rDNA construct itself does not meet the veterinary biologic definition <u>APHIS/VS/CVB</u>	<u>USDA/APHIS/VS/CVB</u>
Medical device for animals	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>FDA/CVM</u>	<u>FDA/CVM</u>	<u>FDA/CVM</u>

⁶ FDA/CBER and FDA/CDRH each have regulatory responsibility for certain medical devices. While FDA/CDRH has regulatory responsibility for most medical devices, FDA/CBER has regulatory responsibility for medical devices related to licensed blood and cellular products. For additional information regarding the division between FDA/CDRH and FDA/CBER of regulatory responsibility for medical devices, please see *Intercenter Agreement Between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health*, available at <http://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm121175.htm>.”

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	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Cosmetics	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk <u>FDA/CFSAN</u>	<u>FDA/CVM</u> <u>FDA/CFSAN</u>	<u>FDA/CFSAN</u>
Industrial or consumer chemicals, including pesticide intermediates	<u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk	<u>FDA/CVM</u>	<u>EPA/OPPT</u> ⁷ If GE microbe is intergeneric, and there are commercial production purposes or if it is for commercial R&D ⁹ , and if it is not excluded under TSCA, ⁸ nor exempt from reporting ¹⁰

⁷ EPA/OPPT regulates certain microbes that make chemical substances or participate in biomass conversion that require TSCA oversight. In some cases, after being employed for these uses, a microbe could enter a separate process flow that leads to use as a component of animal food or cosmetics. In those cases, EPA provides oversight for the TSCA use of the microbe, not the animal food or cosmetic use. The latter are seen as separate uses excluded from review under TSCA.

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Product Area	Source Organism or Culture		
	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Biomass conversion for chemical production, microbial fuel cells, mining and resource extraction, building materials, waste remediation and pollution control, non-pesticidal agriculture applications like biofertilizers, weather and climate modification, various consumer products, and all other applications of intergeneric GE microbes not otherwise excluded under TSCA ⁸			<p><u>EPA/OPPT</u>⁷</p> <p>If GE microbe is intergeneric, and there are commercial production purposes or if it is for commercial R&D,⁹ and if it is not excluded under TSCA,⁸ nor exempt from reporting¹⁰</p>

⁸ New chemical substances made using biotechnology may have both TSCA uses and other non-TSCA uses. EPA reviews only the TSCA uses of such chemicals. Exclusions from TSCA are food, food additives, drugs, cosmetics, medical devices, pesticides (but not pesticide intermediates), tobacco, nuclear material, and firearms. See TSCA Section 3(2)(B).

⁹ Commercial R&D means that the activities are conducted with the purpose of obtaining an immediate or eventual commercial advantage and it includes R&D funded directly by a commercial entity regardless of who is actually conducting the research and R&D not funded directly by a commercial entity, if the researcher intends to obtain an immediate or eventual commercial advantage

¹⁰ A person who manufactures, imports, or processes a microorganism is not subject to reporting requirements if the microorganism is solely for research and development activities; the microorganism is used by, or directly under the supervision of, a technically qualified individual (TQI) defined in §725.3 and the TQI maintains documentation of the procedures selected to ensure compliance; there is no intentional testing of a microorganism outside of a building or vessel which effectively surrounds and encloses the microorganism and includes features designed to restrict the microorganism from leaving; and there are containment and/or inactivation controls. See 40 C.F.R. §§ 275.234-275.235.

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	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>
Other (non-food, non-chemical producing, non-drug producing, non-biologic producing, non-pesticidal organisms)	<u>USDA/APHIS/BRS</u> For ornamental, silvicultural, or turfgrass crops, if GE plant poses a plant pest risk <u>USDA/APHIS/PPQ</u> For ornamental, silvicultural, or turfgrass crops, if GE plant poses plant noxious weed risk	<u>FDA/CVM</u> <u>USDA/APHIS/BRS</u> If GE animal poses a plant pest risk <u>USDA/APHIS/VS</u> If GE animal poses health risk to livestock ⁴	<u>USDA/APHIS/BRS</u> If plant-associated GE microorganism poses a plant pest risk <u>EPA/OPPT</u> If GE microbe is intergeneric, and there are commercial production purposes or if it is for commercial R&D, ⁹ and if it is not excluded under TSCA, ⁸ nor exempt from reporting ¹⁰

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	<i>Genetically Engineered (GE) Plant</i>	<i>Genetically Engineered (GE) Animal</i>	<i>Genetically Engineered (GE) Microbe or Cultured Cell</i>	<i>Cell-free Synthesis</i>
Pesticide ¹¹	<p><u>EPA/OPP</u> If plant-incorporated protectant is produced by GE plant, EPA/OPP regulates the pesticide trait and related genetic material for human and environmental safety and for pesticide residue food/feed safety</p> <p><u>USDA/APHIS/BRS</u> If GE plant poses a plant pest risk</p> <p><u>FDA/CFSAN</u> If human food, FDA/CFSAN oversees non-EPA-regulated aspects of the food for safety for human consumption</p> <p><u>FDA/CVM</u> If animal food, FDA/CVM oversees non-EPA-regulated aspects of the food for safety for animal consumption</p>	<p><u>EPA/OPP</u> If a GE animal is used as a pesticide, EPA/OPP ensures food/feed safety by regulating as chemical pesticide residues any animals or animal parts in the food/feed, e.g., predatory insects, predatory insect parts, or nematodes in grain.</p> <p><u>USDA/APHIS/BRS</u> If GE animal poses a plant pest risk</p> <p><u>FDA/CVM</u>¹²</p>	<p><u>EPA/OPP</u> If pesticide is a GE microbe, EPA/OPP regulates the GE microbial pesticide for human and environmental safety and for pesticide residue food/feed safety. This also includes GE bacterial symbionts that are part of a nematode-bacterial entomopathogen complex.</p> <p><u>USDA/APHIS/BRS</u> If GE microbe poses a plant pest risk</p> <p><u>EPA/OPPT</u> Evaluates and potentially regulates a living GE microbe used as a pesticide intermediate, i.e., where the “pesticide” product is the dead GE microbe</p>	<p><u>EPA/OPP</u> If nucleic acids produced via cell-free synthesis are used for pesticidal purposes,¹³ these products are regulated by EPA/OPP for human and environmental safety and for food/feed safety</p>

¹¹ For certain antimicrobial uses, the antimicrobial is considered both a food additive and a pesticide under the Antimicrobial Regulation Technical Corrections Act of 1998 (ARCTA) with pesticide residue food safety regulated by FDA under the Federal Food, Drug, and Cosmetics Act (FD&C Act), and human and environmental safety regulated by EPA under FIFRA, e.g. antimicrobials to preserve water contacting food where food processing occurs and food packaging preservatives.

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- ¹² As explained in FDA Guidance for Industry 187, “[t]he rDNA construct in a GE animal that is intended to affect the structure or function of the body of the GE animal, regardless of the intended use of products that may be produced by the GE animal, meets the [FD&C Act] drug definition. A non-heritable rDNA construct that is intended to affect the structure or function of a GE animal or to cure, mitigate, or treat a disease in the animal also meets the drug definition.” FDA is discussing with other agencies the best approach for oversight of GE insects. Future guidance may be developed to address them. Until guidance is issued, oversight of GE insects will be determined on a case-by-case basis.
- ¹³ Examples of such pesticidal applications include double stranded RNA used for RNAi gene silencing.